



PATENT

Attorney Docket No. DIVER1280

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Short and Keller

Art Unit: 1652

Serial No.: 08/876,276

Examiner: P. Tung R Am REZ

Filed: June 16, 1997

Title: HIGH THROUGHPUT SCREENING FOR NOVEL ENZYMES

Commissioner for Patents
Washington, D.C. 20231

TRANSMITTAL SHEET

Sir:

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Transmitted herewith for the above-identified application please find:

1. Information Disclosure Statement; (2 pgs.)
2. Form PTO-1449; (1 pg.)
3. Four (4) References;
5. Check \$180.00 (check # 505408)
6. Return Postcard

Date of Deposit April 8, 2002

I hereby certify that this paper is being deposited with the United States Postal Service "First-Class Mail Post Office to Addressee" service under 37 CFR 1.08 on the date indicated above and is addressed to, Commissioner of Patents and Trademarks; Washington, DC 20231.

Jason Berry Jason Berry

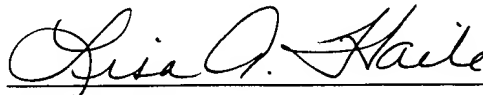
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Page 2

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A check in the amount of \$180.00 is enclosed to cover the fee to file the Information Disclosure Statement. The Commissioner is hereby authorized to charge any additional fees required by this filing, or credit any overpayment, to Deposit Account No. 50-1355. A copy of the transmittal sheet is enclosed.

Respectfully submitted,

Date: 4/8/02



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INFORMATION DISCLOSURE STATEMENT

Sir:

In accordance with 37 C.F.R. 1.97, enclosed are additional references relating to the above-identified application. For the convenience of the Examiner, these references are listed on the attached Form PTO-1449 and a copy of each is enclosed herewith.

It is respectfully requested that these references be considered in the examination of this application and their consideration be made of written record in the application file.

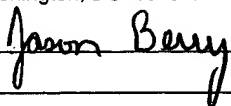
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21. Nov. 2000

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bearb.:

Datum/Date

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Anmeldung Nr./Application No./Demande n°/Patent Nr./Patent No./Brevet n°

98931354.9-2116/US9812674

Anmelder/Applicant/Demandeur/Patentinhaber/Proprietor/Titulaire

Diversa Corporation

COMMUNICATION

The European Patent Office herewith transmits the partial European search report under Rule 46(1) EPC relating to the above-mentioned European patent application.

Copies of the documents cited in the search report are enclosed.

The applicant's attention is drawn to the following:

The search Division informs the applicant that if the European search report is also to cover inventions other than the invention first mentioned in the claims, a further search fee must be paid for each of these inventions, within ONE MONTH after notification of this communication.

If the application has been filed up to 30 June 1999, the search fee in force before 01 July 1999 (EUR 869,-) or the equivalent applicable on the date of payment is payable.

This applies also to the search fees requested under Rule 46(1) EPC.

See also OJ EPO 06/1999, 405.

☐ The abstract was modified by the Search Division and the definitive text is attached to the present communication.

☒ Additional set(s) of copies of the documents cited in the European search report is (are) enclosed as well.



Note to users of the automatic debiting procedure:

Unless the EPO receives prior instructions to the contrary, the search fee(s) will be debited on the last day of the period for payment. For further details see the Arrangements for the automatic debiting procedure, Supplement to OJ EPO 02/1999.

REGISTERED LETTER



European Patent
Office

**SUPPLEMENTARY
PARTIAL EUROPEAN SEARCH REPORT**

Application Number

under Rule 46, paragraph 1 of the European Patent Convention EP 98 93 1354

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.6)
Y	WO 96 34112 A (CHROMAXOME CORP) 31 October 1996 (1996-10-31) * page 68, line 1 - page 71, line 37 * * page 84, line 30 - page 86, line 8; claims 1-41; figure 8 * * page 88, line 6 - page 89, line 12 * * page 102, line 25; examples 6.2-6.6 * * page 101, line 1 - line 14 * * page 90, line 33 - page 91, line 22 * ---	1-20, 62-64	C12Q1/68 C12N15/10
Y	WO 97 04077 A (MARRS BARRY ;SHORT JAY M (US); STEIN JEFFREY L (US); RECOMBINANT B) 6 February 1997 (1997-02-06) * page 11, line 13 - page 12, line 4; claim 8 * ---	62-64	
Y	WO 97 20078 A (AFFYMAX TECH NV ;CRAMERI ANDREAS (US); STEMMER WILLEM P C (US)) 5 June 1997 (1997-06-05) * the whole document * ---	62,64	
			TECHNICAL FIELDS SEARCHED (Int.Cl.6)
			C12N C12Q
LACK OF UNITY OF INVENTION			
The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:			
see sheet B			
The present partial European search report has been drawn up for those parts of the European patent application which relate to the invention first mentioned in the claims.			
Place of search		Date of completion of the search	Examiner
THE HAGUE		31 October 2000	Hornig, H
CATEGORY OF CITED DOCUMENTS			
X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document		T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons ----- & : member of the same patent family, corresponding document	

2

EPO FORM 1503 03.92 (P04C23)



DOCUMENTS CONSIDERED TO BE RELEVANT			CLASSIFICATION OF THE APPLICATION (Int.Cl.6)
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	
D,A	WITTRUP K D ET AL: "Microencapsulation selection for isolation of yeast mutants with increased secretion of Aspergillus awamori glucoamylase." BIOTECHNOLOGY AND BIOENGINEERING, vol. 42, no. 3, 1993, pages 351-356, XP002151519 ISSN: 0006-3592 * the whole document *		
A	ROESSNER CHARLES A ET AL: "Fluorescence-based method for selection of recombinant plasmids." BIOTECHNIQUES, vol. 19, no. 5, 1995, pages 760, 762-764, XP002151562 ISSN: 0736-6205 * the whole document *		TECHNICAL FIELDS SEARCHED (Int.Cl.6)
P,A	WO 97 48717 A (RECOMBINANT BIOCATALYSIS INC) 24 December 1997 (1997-12-24) * the whole document *		
2			



The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

1. Claims: 1-20,62-64

A method for identifying bioactivities or biomolecules using high throughput screening of genomic DNA samples to identify one or more enzymes encoded by the DNA of said sample, comprising: a) providing an expression library containing a plurality of clones, wherein the DNA for generating the library is obtained from a mixed population of organism; b) inserting bioactive fluorescent substrate in at least one clone of the library wherein the substrate is fluorescent in the presence of a bioactivity or biomolecule; c) screening the clones with a fluorescent analyzer that detects bioactive fluorescence; and d) identifying clones detected as positive for bioactive fluorescence, wherein fluorescence is indicative of DNA that encodes an bioactivity or biomolecule; said method, wherein the sample is encapsulated in a gel microdrop; said method, wherein the expression library contains DNA from extremophiles; said method, wherein the bioactive substrate comprises C12FDG; said method including the additional steps of: subjecting an enzyme encoded by the DNA identified in step d) to directed evolution comprising the step of: a) subjecting the enzyme to non-directed mutagenesis; and b) screening mutant enzymes produced in step a) for a mutant enzyme; said method for identifying bioactivities or biomolecules using high throughput screening of genomic DNA in a culture-independent system; said method further comprising encapsulation the clones and the bioactive substrate prior to screening; said method wherein the expression library is procaryotic.

2. Claims: 21-27

A method of screening for an agent that modulates the activity of a target cell component, wherein the target cell component and a selectable marker are expressed by a recombinant cell, the method comprising co-encapsulating the agent in a micro-environment with the recombinant cell expressing the target cell component and detectable marker and detecting the effect of the agent on the activity of the cell component; said method wherein the agent is a transducing protein, said protein is a G-protein;

3. Claims: 28-46

A method for enriching for target DNA sequences containing at least a partial coding region for at least one specified activity in a DNA sample comprising: a) co-encapsulating in a micro-environment a mixture of target DNA obtained from a mixture of organisms with a mixture of target DNA probes comprising a detectable marker and at least a portion of a DNA sequence encoding at least one enzyme having a specified



The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

enzyme activity; b) incubating the co-encapsulated mixture under such conditions and for such time as to allow hybridization of complementary sequences; and c) screening for the specified activity;

4. Claims: 47-61

A method of screening for an agent that modulates the interaction of a first test protein linked to a DNA binding moiety and a second test protein linked to a transcriptional activation moiety, comprising co-encapsulating the agent with the first test protein and second test protein in a suitable microenvironment and determining the ability of the agent to modulate the interaction of the first test protein linked to a DNA binding moiety with the second test protein covalently linked to a transcriptional activation moiety, wherein the agent enhances or inhibits the expression of a detectable protein, and wherein the enhancement or inhibition is detected by FACS analysis;

**ANNEX TO THE EUROPEAN SEARCH REPORT
ON EUROPEAN PATENT APPLICATION NO.**

EP 98 93 1354

This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report.
The members are as contained in the European Patent Office EDP file on
The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

31-10-2000

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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